

(b) detecting an interaction between heavy or light chain polypeptides of the first and second repertoires, thereby identifying those members of the first repertoire that interact with members of the second repertoire.

57. (New) The method of claim 56, wherein said first and second repertoires are each present in a series of continuous, non-intersecting lines.

58. (New) The method of claim 56, wherein said heavy or light chain polypeptide is a domain antibody (dAb).

59. (New) The method of claim 56, wherein said first repertoire comprises V_H or V_L .

60. (New) The method of claim 56, wherein said second repertoire comprises V_H or V_L .

61. (New) The method of claim 56, wherein said first repertoire comprises V_H , and said second repertoire comprises V_L .

62. (New) The method of claim 56, wherein said step of detecting comprises contacting said at least one array with a target epitope, and detecting binding of the target epitope by juxtaposed members of said first and second repertoires on said array, wherein said binding of the target antigen is indicative of an interaction of members of said first and second repertoire.

63. (New) The method of claim 56, wherein said step of detecting comprises contacting said at least one array with a third repertoire of target antigen members arranged in a series of continuous lines, and detecting binding of target antigen by juxtaposed members of said first and second repertoires at positions on said array, wherein said binding of target antigen is indicative of an interaction of members of said first and second repertoire.

64. (New) The method of claim 63, wherein a plurality of lines of said third repertoire comprise a different target antigen.

65. (New) The method of claim 56, wherein each line of said at least two series of lines is present in a channel provided in a solid material such that a plurality of channels containing a

member of the first repertoire intersects a plurality of channels containing a member of the second repertoire.

66. (New) The method of claim 56, wherein members of the first and second repertoires are applied to a single support.

67. (New) The method of claim 56, comprising the steps of:

(a) arranging the first repertoire on a first support in a series of continuous lines and arranging the second repertoire on a second support in a series of continuous lines;

(b) juxtaposing the first and second supports such that a plurality of members of the first repertoire are juxtaposed with a plurality of members of the second repertoire to form said array; and

(c) detecting an interaction between members of the first and second repertoires.

68. (New) The method of claim 67, wherein said first and second repertoire are each arranged in a series of continuous, non-intersecting lines.

69. (New) A method for creating a combinatorial library of polypeptides comprising two chains, each member of which library comprises one member of a first repertoire of members comprising a heavy and/or light chain polypeptide and one member of a second repertoire of members comprising a heavy and/or light chain polypeptide, which method comprises the step of arranging the first repertoire of members in a first series of continuous lines, and said second repertoire in a second series of continuous lines, such that a plurality of members of the first repertoire are juxtaposed to a plurality of members of the second repertoire, thereby generating at the points of juxtaposition, a plurality of combinations of polypeptides comprising two chains, thereby creating a combinatorial library of polypeptides comprising two chains.

70. (New) The method of claim 69, wherein said first and second repertoires are each arranged in a series of continuous, non-intersecting lines.

71. (New) The method of claim 69, wherein said heavy or light chain polypeptide is a domain antibody (dAb).
72. (New) The method of claim 69, wherein said first repertoire comprises V_H or V_L .
73. (New) The method of claim 69, wherein said second repertoire comprises V_H or V_L .
74. (New) The method of claim 69, wherein said first repertoire comprises V_H , and said second repertoire comprises V_L .
75. (New) A method of screening the combinatorial library of two-chain polypeptides of claim 69 for binding to a target molecule, the method comprising the step of detecting an interaction between the two chain polypeptides and the target molecule.
76. (New) The method of claim 75, wherein said step of detecting comprises contacting said combinatorial library of two chain polypeptides with a third repertoire of target antigen members arranged in a series of continuous lines such that a plurality of members of said first, second, and third repertoire is juxtaposed to a plurality of other members of said first, second, and third repertoire, and detecting binding of target antigen by juxtaposed members of said first and second repertoires, wherein said binding of the target antigen is indicative of an interaction of members of said first and second repertoire.
77. (New) The method of claim 76, wherein said first, second and third repertoires are each arranged in a series of continuous, non-intersecting lines.
78. (New) The method of claim 56, 62, 63, 69, 75, or 76 whereby one or more of the first, second and, if present, third repertoires are provided by a plurality of nucleic acid sequences which encode said heavy or light chain polypeptide of said first and second repertoires or said target epitope of said third repertoire and which are expressed to produce their corresponding polypeptides *in situ* in the array.

79. (New) The method according to claim 78, wherein the nucleic acid sequences are provided by expression vectors which encode polypeptide members of the repertoire, and are operatively linked to control sequences sufficient to direct the transcription of the nucleic acid molecules.
80. (New) The method of claim 79, wherein the expression vector is a bacteriophage.
81. (New) The method of claim 79, wherein the expression vector is a plasmid.
82. (New) The method of claim 79, wherein the expression vector is a linear nucleic acid molecule.
83. (New) The method of claim 79, wherein the nucleic acids are contained and expressed within cells.
84. (New) The method according to claim 83, wherein the cells are selected from the group consisting of bacterial cells, lower eukaryotic cells and higher eukaryotic cells.
85. (New) The method of claim 78, wherein the nucleic acid molecules are immobilized in the form of naked or complexed nucleic acid.
86. (New) The method of claim 56, 62, 63, 69, 75, or 76, wherein the members of at least one repertoire are arrayed using robotic means.
87. (New) A method of screening a first repertoire of members comprising a heavy or light chain polypeptide against a second repertoire of members comprising a heavy or light chain polypeptide to identify those members of the first repertoire which do not interact with members of the second repertoire, the method comprising:
- (a) arranging the first and second repertoires in at least two series of continuous lines to form an array, such that a plurality of members of the first repertoire are juxtaposed with a plurality of members of the second repertoire; and

(b) identifying those members of the first and second repertoires that do not interact with one another.

88. (New) The method of claim 87, wherein said first and second repertoires are each arranged in a series of continuous, non-intersecting lines.

89. (New) The method of claim 87, wherein said heavy or light chain polypeptide is a domain antibody (dAb).

90. (New) The method of claim 87, wherein said first repertoire comprises V_H or V_L .

91. (New) The method of claim 87, wherein said second repertoire comprises V_H or V_L .

92. (New) The method of claim 87, wherein said first repertoire comprises V_H , and said second repertoire comprises V_L .

93. (New) A method of screening a first repertoire of members comprising a heavy or light chain polypeptide against a second repertoire of members comprising a heavy or light chain polypeptide to identify members of the first and second repertoires whose interactions with one another are dependent on the presence or absence of a third molecule or set of molecules, comprising:

(a) arranging the first and second repertoires in at least two series of continuous lines to form an array, such that a plurality of members of the first repertoire are juxtaposed with a plurality of members of the second repertoire; and

(b) detecting an interaction between juxtaposed members of the first repertoire and members of the second repertoire in the presence of the third molecule or set of molecules, such that members of the first and second repertoires whose interactions with one another are dependent on the presence or absence of the third molecule or set of molecules are identified.

94. (New) The method of claim 93, wherein said first and second repertoires are each arranged in a series of continuous, non-intersecting lines.

95. (New) The method of claim 93, wherein said heavy or light chain polypeptide is a domain antibody (dAb).

96. (New) The method of claim 93, wherein said first repertoire comprises V_H or V_L .

97. (New) The method of claim 93, wherein said second repertoire comprises V_H or V_L .

98. (New) The method of claim 93, wherein said first repertoire comprises V_H , and said second repertoire comprises V_L .

99. (New) The method of claim 93, wherein said third molecule or set of molecules is present at varying concentrations.

100. (New) A method for screening a peptide repertoire comprising a heavy or light chain polypeptide against the same peptide repertoire to identify those members of the peptide repertoire that interact with other members of the peptide repertoire, which method comprises:

(a) arranging the members of the peptide repertoire in at least two series of continuous lines to form at least one array, such that a plurality of the members of the peptide repertoire are juxtaposed to one another; and


(b) detecting the interaction of different juxtaposed members of the peptide repertoire, whereby those members of the peptide repertoire that interact with other members of the peptide repertoire are identified.

101. (New) The method of claim 100, wherein said heavy or light chain polypeptide is a domain antibody (dAb).

102. (New) The method of claim 100, wherein said peptide repertoire comprises V_H .

103. (New) The method of claim 100, wherein said peptide repertoire comprises V_L .

104. (New) A method for creating a combinatorial library consisting of all members of a first repertoire of polypeptides paired with all members of a second repertoire of polypeptides, which method comprises:

 (a) arranging a plurality of host cells containing a plurality of nucleotide sequences encoding a first repertoire of heavy or light chain polypeptides in a first series of continuous lines, and a plurality of viruses containing a plurality of nucleotide sequences encoding a second repertoire of heavy or light chain polypeptides in a second series of continuous lines to create an array, such that lines comprising cells containing a plurality of nucleotide members of the first repertoire intersect with lines comprising viruses containing a plurality of nucleotide members of the second repertoire;

(b) infecting the cells containing the nucleotide members of the first repertoire with the viruses that contain the nucleotide members of the second repertoire where the two repertoires intersect; and

(c) expressing the nucleotide sequences to produce the corresponding polypeptides of the first and second repertoires, thereby creating a combinatorial library consisting of a plurality of members of the first repertoire of polypeptides paired with a plurality of members of the second repertoire of polypeptides.

105. (New) The method of claim 104, wherein said first repertoire and second repertoire are each arranged in a series of continuous, non-intersecting lines.

106. (New) The method of claim 104, wherein said heavy or light chain polypeptide is a domain antibody (dAb).

107. (New) The method of claim 104, wherein said first repertoire comprises V_H or V_L .

108. (New) The method of claim 104, wherein said second repertoire comprises V_H or V_L .

109. (New) The method of claim 104, wherein said first repertoire comprises V_H , and said second repertoire comprises V_L .

110. (New) A method of screening the combinatorial library created according to the method of claim 104 to identify members of the first repertoire that interact with members of the second repertoire, said method comprising the step of detecting an interaction between polypeptide members of the first and second repertoires, whereby members of the first repertoire that interact with members of the second repertoire are identified.

111. (New) A method for creating a yeast two hybrid library consisting of all members of a first repertoire of heavy or light chain polypeptides paired with all members of a second repertoire of heavy or light chain polypeptides, which method comprises:

(a) arranging yeast cells containing a plurality of nucleotide sequences encoding a first repertoire of heavy or light chain polypeptides, and yeast cells containing a plurality of nucleotide sequences encoding a second repertoire of heavy or light chain polypeptides each in a series of continuous lines to create an array, such that a plurality of yeast cells containing nucleotide members of the first repertoire intersect with a plurality of yeast cells containing nucleotide members of the second repertoire;

(b) allowing the yeast cells containing the members of the first repertoire to mate with juxtaposed yeast cells containing the members of the second repertoire; and

(c) expressing the nucleotide sequences to produce the corresponding heavy or light chain polypeptide of the first and second repertoires, thereby creating a yeast two hybrid library consisting of a plurality of members of a first repertoire of polypeptides paired with a plurality of members of a second repertoire of polypeptides.

112. (New) The method of claim 111, wherein said yeast cells comprising said first repertoire and said yeast cells comprising said second repertoire are each arranged in a series of continuous, non-intersecting lines.

113. (New) The method of claim 111, wherein said heavy or light chain polypeptide is a domain antibody (dAb).

114. (New) The method of claim 111, wherein said first repertoire comprises V_H or V_L .

115. (New) The method of claim 111, wherein said second repertoire comprises V_H or V_L .

116. (New) The method of claim 111, wherein said first repertoire comprises V_H , and said second repertoire comprises V_L .

117. (New) A method of screening a combinatorial library created according to the method of claim 111 to identify members of the first repertoire that interact with members of the second repertoire, the method comprising the step of detecting an interaction between the polypeptide members of the first and second repertoires, whereby members of the first repertoire that interact with members of the second repertoire are identified.

Remarks

Claims 1-55 are currently pending in the application. Upon entry of this amendment, claims 1-55 will be canceled and claims 56-117 will be added. Support for newly added claims 56-117 may be found in the specification and claims as originally filed. Specifically, support for the recitation of "heavy or light chain polypeptide" may be found on page 10, line 34 through page 11, line 7. Particularly, the specification teaches that a heavy or light chain polypeptide may be V_H or V_L , or may be an antibody fragment including a "heavy chain, a light chain, a heavy chain-light chain dimer, a Fab fragment, a $F(ab')_2$ fragment, a dAb fragment, a light or heavy chain single domain, and an Fv fragment, including a single chain Fv (scFv) or a di-sulphide bonded Fv (dsFv)".

Applicants submit that the relationship of newly filed claims to the Groups set forth in the Restriction Requirement mailed on November 1, 2002 is as follows. The claims elected in Applicants response to the Restriction Requirement filed herewith are indicated in **bold**, and the claims which Applicants respectfully submit are improperly restricted and should be rejoined are